Influence of Autonomic Nervous Activity on Variations in the R-R Intervals in Adult Goats

Kanji MATSUI and Shigeru SUGANO
Animal Husbandry Experiment Station, Faculty of Agriculture, The University of Tokyo, Iwama, Ibaraki 319-02 and Department of Animal Environmental Physiology, Faculty of Agriculture, The University of Tokyo, Bunkyo-ku, Tokyo 113, Japan

(Received 26 October 1988/Accepted 8 February 1989)

ABSTRACT. We used a heart rate memory apparatus to measure 2047 successive R-R intervals with an accuracy of 10 msec in adult goats. For 100 successive stationary R-R intervals out of the 2047 intervals, the R-R intervals sequence was recorded graphically and the means and standard deviations (SD) were calculated. The magnitude of the variation in the R-R intervals was represented by the SD. The usefulness of the analysis of R-R intervals as an indicator of autonomic nervous activity was determined. The diagram of 100 successive R-R intervals at rest showed a conspicuous periodic fluctuation. After the administration of atropine, atropine plus propranolol or after feeding, the R-R intervals were markedly shortened and the variations in the R-R intervals were abolished. After the administration of propranolol only, the R-R intervals were prolonged and the amplitude of the fluctuations in the R-R intervals was conspicuously increased. The respiration curve and the variation in the R-R intervals at rest fluctuated in periodic synchrony. A positive correlation between the mean and the SD of the R-R intervals was highly significant. This indicates that the variations in the R-R intervals in adult goats are closely related to autonomic nervous activity and that the analysis of the R-R intervals is suitable for the noninvasive assessment of autonomic nervous activity.—KEY WORDS: autonomic nervous activity, goat, R-R interval.


It is generally known that heart rate (HR) is not held constant, but changes easily with time. This phenomenon is called variation in R-R interval, beat-to-beat variation or heart rate variation. The R-R intervals are affected by numerous factors including blood pressure, body temperature, respiration, acid-base balance, oxygenation, physical movement and psychological parameters [5, 6]. The variation in the R-R interval can be analyzed by a continuous measurement of the R-R interval.

The R-R interval is widely used for monitoring human [7, 21, 22] and animal [3, 4] fetuses at high risk during pregnancy. The R-R interval is also used to assessing the effects of autonomic nervous activity on cardiac function [1], especially the dysfunction of the autonomic nervous activity in diabetic patients [2, 17, 23].

We have assessed an autonomic nervous tone at rest in various domestic animals using HR after the administration of autonomic blockers [10, 11, 12]. However, it is necessary to provide a noninvasive and quantitative method of assessing autonomic nervous activity to the heart. In the present study, therefore the relationship between variation in the R-R intervals and autonomic nervous activity was examined in adult goats by the computer analysis of 100 successive R-R intervals.

MATERIALS AND METHODS

Animals and operative procedure: Three healthy adult female Shiba goats [9] were used in this study. They were 2.5 to 3.0
years old and weighed 23 to 28 kg. Throughout the experiment they were tied to stanchions and fed twice a day. Water was supplied ad libitum. They were accustomed to stanchions before the experiment. The goats were operated under anesthesia to implant subcutaneously three handmade stainless steel electrodes for electrocardiogram (ECG) in an A-B lead. The electrodes for the bipolar A-B lead were attached along the longitudinal heart axis; the positive electrode was placed at the apex and the negative electrode at the base of the heart [19]. In one of the three goats, a thermister respiratory sensor was implanted in the trachea for pneumotachography.

**Measurement of HR and R-R interval for 24 hr:** The ECG and pneumotachogram were monitored for 24 hr using a 4-channel telemeter (Multitelemeter 511, NEC Sanei) and stored on a cassette data recorder (R-61, Teac). HR (beats/min) and R-R intervals (sec) were measured directly from the output of the multitelemeter, or indirectly from stored data using a heart rate memory apparatus (Nos. 1850a and 1850e, Takei Scientific Instruments). This apparatus consisted of a data logger, an interface and a microcomputer (PC-9801 VM2, NEC). It measured and stored 2047 successive R-R intervals with an accuracy of 10 msec, or the number of heart beats at intervals of 10 sec, 30 sec or 60 sec. The 2047 successive R-R intervals were measured at intervals of 3 to 4 hr during 24 hr. Artifactual R-R intervals were identified by examining the original ECG records. HR and R-R interval data were analyzed and the diagrams for HR during 24 hr and 2047 successive R-R intervals were constructed by the microcomputer.

The diagrams for the 100 R-R intervals were drawn on the time series of the R-R intervals and the means and standard deviations (SD) were calculated from the 100 R-R intervals. The magnitude of the variation in the R-R interval was indicated by the SD.

**Changes in R-R intervals after autonomic blockade:** Selective blockade of the parasympathetic (muscarinic) and sympathetic (beta-adrenergic) nerves was accomplished with atropine sulphate (Sigma Chemicals) and propranolol (Sigma Chemicals), respectively. A single dose of atropine (0.3 mg/kg) or propranolol (1.0 mg/kg), or a combined dose of both drugs was injected into the jugular vein as indicated in our previous reports [11]. The variations in the R-R intervals before and after the blockade were compared. Moreover, the R-R intervals were examined during feeding normally and during feeding after the administration of propranolol.

**RESULTS**

**Diurnal pattern in HR (Fig. 1):** The HR was lower from midnight to early morning (60 beats/min) and higher during the daytime (80 beats/min). Feeding greatly increased the HR, to 150 beats/min. A transient increase in HR accompanied the act of standing up. The diurnal patterns in HR were basically similar among the three goats.

**Typical trace records of 2047 and 100 successive R-R intervals (Fig. 2):** The baseline in the diagram of 2047 successive R-R intervals diverged several times during the observation period. The diagram of 100 successive R-R intervals showed a conspicuous periodic fluctuation. The mean and SD of the R-R intervals were 0.897 and 0.055 (sec), respectively.

**Examples of records of 100 successive R-R intervals (Fig. 3):** Fluctuations were shown in the records at 4: 15 a.m. and 10: 30 a.m. The amplitudes of the fluctuations were larger at 4: 15 a.m. than at 10: 30 a.m. The fluctuations were abolished at feeding time (9: 00 a.m). The magnitude of the mean and
SD of the R-R intervals ranked in decreasing order from 4:15 a.m. to 10:30 a.m. to feeding time.

Variations in 100 successive R-R intervals after autonomic blockade (Figs. 4 and 5): After the administration of atropine or atropine plus propranolol, the R-R intervals were shortened and their variations were almost abolished. But after the administration of propranolol the R-R intervals were prolonged and the amplitude in the fluctuations of the R-R intervals increased conspicuously. Figure 5 shows the recovery process during 45 min after the administration of atropine. Just after the administration, the R-R intervals were markedly shortened.
R-R INTERVALS AND AUTONOMIC NERVOUS ACTIVITY

Fig. 3. Diagrams of 100 successive R-R intervals. Figure shows examples of records of long, middle and short R-R intervals. Top panel: the record at 4:15 a.m. (mean±SD: 1.011±0.085 sec). Middle panel: the record at 10:35 a.m. (0.740±0.039 sec). Bottom panel: the record at feeding time at 9:00 a.m. (0.367±0.006 sec).

Fig. 4. Changes in the variations in 100 successive R-R intervals after autonomic blockade. Top panel: before (left panel; mean±SD of the 100 R-R intervals: 0.938±0.078 sec) and after (right panel; 0.420±0.007 sec) the administration of atropine. Middle panel: before (left panel; 0.742±0.046 sec) and after (right panel; 0.983±0.086 sec) the administration of propranolol. Bottom panel: before (left panel; 0.798±0.041 sec) and after (right panel; 0.510±0.006 sec) the administration of atropine plus propranolol.
and their variations were almost abolished until 16 min after the administration when the R-R intervals gradually became prolonged, but hardly any variations reappeared. Thereafter, the R-R intervals were markedly prolonged and the variations recovered only gradually.

Breathing and variations in R-R intervals (Fig. 6): The respiration curve and the fluctuations in the R-R intervals varied synchronously. The inspiratory phase was accompanied with a shortening of the R-R intervals and the expiratory phase with a prolongation of the R-R intervals.

Changes in HR during feeding with and without sympathetic blockade (Fig. 7): Feeding induced a marked increase in HR (tachycardia) as shown in Fig. 1. However, the administration of propranolol before feeding almost blocked the tachycardia caused by feeding.

Correlation between the mean and SD of 100 successive R-R intervals (Fig. 8): All data plotted in Fig. 8 are from one goat. The SD (y) showed a highly significant positive correlation with the mean (x) of R-R intervals. The equation for the regression line was \( y = 0.132x - 0.047 \) (\( r = 0.960, p < 0.001, n = 13, \text{unit: sec} \)). The level and slope of the straight line were similar to those from the other goats.
R-R INTERVALS AND AUTONOMIC NERVOUS ACTIVITY

Fig. 7. Heart rates at feeding with and without the beta-sympathetic blockade. Note that the tachycardia accompanying feeding is almost blocked by the propranolol. Left panel: normal feeding (without the administration of propranolol). Right panel: feeding with the administration of propranolol (PR). The open and solid symbols (circle, triangle and square) show the same animal.

Fig. 8. Correlation between the mean and SD of 100 successive R-R intervals. The SD (y) shows a highly significant positive correlation with the mean (x). The equation for the line is y=0.132x−0.047 (r=0.960, p<0.001, n=13, unit: sec). The right upward direction in the figure indicates an increase in parasympathetic activity and the left downward direction indicates an increase in beta-sympathetic activity.

DISCUSSION

Fluctuations in R-R intervals were studied in our country 20 years ago in rabbits [20], dogs [14, 15] and horses [16, 18]. These pioneering works were very suggestive. That is, they were concerned with the time series analysis of the R-R intervals [20], influence of exercise on R-R intervals [14], or with radiotelemetry techniques [14, 16, 18]. Regrettably, hardly any such studies continued after that, to our knowledge. Recently, it is thought that the variations in the R-R intervals result from rapid alterations in autonomic effects on the heart. Basic studies have been performed in human fetuses [7, 21, 22], newborn [5], fetal lambs [3, 4] and puppies and dogs [6]. On the other hand, the variation of the R-R intervals is continuously measured over 24 hr by Ninomiya et al. [13], the inverse value of the R-R interval is used as an index of the frequency of ventricular excitation rhythm.

The present results indicate that the R-R intervals in adult goats fluctuate fundamentally as shown in Figs. 2 and 3. The magnitude of the variations in R-R intervals may be expressed as the SD of the R-R intervals [3, 6]. To characterize the influences of autonomic activity on the variations in the R-R interval, we varied the level of autonomic activity by the use of pharmacological blockade, by feeding and by
observing diurnal effects during 24 hr. The administrations of atropine, atropine plus propranolol or the process of feeding markedly shortened the R-R intervals and abolished the variations in the R-R intervals. That is, the mean and SD of 100 successive R-R intervals were extremely reduced. It is also demonstrated in Fig. 5 that as the parasympathetic activity recovers to its level before the administration of atropine, the R-R intervals gradually become longer and the magnitude of the variations become larger. With feeding (Figs. 1 and 3), the R-R intervals were shortened and their variations were almost abolished. Since the administration of propranolol before feeding nearly blocked the tachycardia induced by feeding, as shown in Fig. 7, the abolishment of the variations in the R-R intervals was considered to result from an increase in the beta-sympathetic activity induced by feeding. On the other hand, the administration of propranolol prolonged the R-R intervals and increased the variations. Therefore, it is concluded that the shortening of the R-R intervals and the abolishment of the variation in the R-R intervals occur when beta-sympathetic activity is dominant.

Figure 8 shows the significant positive correlation between the mean and SD of 100 successive R-R intervals. Thus, the longer the R-R intervals the more they vary. And the right upward direction in the figure indicates an increase in parasympathetic activity and the left downward direction indicates an increase in beta-sympathetic activity. These results suggest that the SD as well as the mean of the R-R intervals in the adult goats is closely related to autonomic nervous activity.

The HR after the administration of atropine plus propranolol (Fig. 4) is defined as the “intrinsic heart rate” without parasympathetic and sympathetic neural regulation, as indicated by Jose [8]. The mean of the R-R intervals after the administration of atropine plus propranolol was larger than that after the administration of atropine alone, whereas the SD of the R-R intervals was extremely small and was almost the same in both cases. Therefore, the variation in the R-R intervals may be influenced by parasympathetic activity with no relation to beta-sympathetic activity.

It is well known that there is a relationship between breathing and variations in the R-R intervals in the fetal [3, 22] and postnatal stages [6]. This phenomenon is generally called a “respiratory sinus arrhythmia,” that is, the R-R intervals are prolonged during expiration and shortened during inspiration. In this situation the parasympathetic activity is considered to be greater than the sympathetic activity, judging from the mean of the R-R intervals. Though this relationship was not assessed in detail in all of the cases, it is confirmed that respiration is one of the critical factors that affect the R-R intervals. This suggests that the variation in R-R intervals is closely related to autonomic nervous activity in the adult goats and that an analysis of R-R intervals should be useful for the noninvasive assessment of autonomic nervous activity.

REFERENCES

146: 456–462.